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EXAMINER	
DAM, DUSTIN Q	
ART UNIT	PAPER NUMBER
1795	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,341	WONG ET AL.	
	Examiner	Art Unit	
	DUSTIN Q. DAM	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/7/2007, 6/6/2005, 4/11/2005, 11/8/2004, & 8/20/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. This is the initial Office Action based on the Electrochemical Detection of NADH or NAPH filed on February 21, 2003.

2. Claims 1-16 are currently pending and have been fully considered.

Specification

3. The disclosure is objected to because of the following informalities: The title recites, "Electrochemical Detection of NADH or ***NAPH***". It is construed that applicant intended to recite "Electrochemical Detection of NADH or ***NADPH***" which is consistent with the specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-6, 13, 15, and 16 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by COSNIER et al. ("*An Original Electroenzymatic System: Flavin Reductase-Riboflavin for the Improvement of Dehydrogenase-Based Biosensors. Application to the Amperometric Detection of Lactate* " Electroanalysis Vol. 9 No. 9 (1997) pages 685-688).

a. With regards to claim 1, COSNIER et al. discloses an electrochemical method for detecting the presence or absence of, or for determining the concentration of, NADH or NADPH in a sample comprising; contacting a reductase (FIG. 2 "flavin reductase") and a redox active agent (FIG. 2 "riboflavin") with said sample; and measuring the quantity of reduced redox active agent (FIG. 2 "dihydroriboflavin") produced by the reductase, by electrochemical means (FIG. 2 discloses schematic for reaction sequence which inherently comprises contacting the above elements and the 2nd paragraph of **3. Results and Discussion**, page 686 discloses "amperometric response" "corresponding to the oxidation of the enzymatically generated dihydroriboflavin").

b. With regards to claim 2, COSNIER et al. discloses a method for monitoring the amount or activity of a redox enzyme or substrate, wherein the redox enzyme (FIG. 2 "dehydrogenase") uses NADP, NADPH or NAD^+, $NADP^+$ as a co-factor (FIG. 2 "$NAD(P)^+$/NAD(P)H") comprising carrying out the method of claim 1, wherein electron transfer between the redox active agent and an electrode is correlated to the amount or activity of the redox enzyme or substrate (FIG. 2 & see 3rd paragraph of **3. Results and Discussion**, page 687).

c. With regards to claim 3, COSNIER et al. discloses a method wherein NADH or NADPH are produced by the reduction of NAD^+ or $NADP^+$ (FIG. 2) by a redox enzyme (FIG. 2 "dehydrogenase") which concomitantly oxidizes a substrate (3rd paragraph of **3. Results and Discussion**, page 687).

d. With regards to claim 4, COSNIER et al. discloses a method wherein the amount of NADH or NADPH formed is proportional to the amount of the redox enzyme present

or the amount of its substrate and hence allows the detection, or quantification, of the enzyme or substrate in the sample (FIG. 2 & see 3rd paragraph of **3. Results and Discussion**, page 687).

e. With regards to claim 5, COSNIER et al. discloses a method wherein the redox enzyme is a dehydrogenase (FIG. 2 "dehydrogenase").

f. With regards to claim 6, COSNIER et al. discloses a method wherein the reductase is capable of accepting two electrons from NADH or NADPH (1st paragraph of **3. Results and Discussion**, page 686 "flavin oxidoreductase (Fre)" is capable of accepting two electrons from NADH or NADPH & also see FIG. 2 and 1st paragraph of **3. Results and Discussion**, page 686 discloses "two-electron transfer from reduced pyridine nucleotides").

g. With regards to claim 13, COSNIER et al. discloses a method which allows (the term "allows" is interpreted to mean, but not limited to, "capable of") a monitoring of the amount of the substrate, enzyme, NADH or NADPH over time (**2.4 Assays** "time dependent").

h. With regards to claim 15 and 16, COSNIER et al. discloses an electrochemical cell which can be used to carry out the method of claim 1 comprising a sample holding means (FIG. 2 "Polymer"), a source of reductase (FIG. 2 "Flavin Reductase"), a redox active agent (FIG. 2 "riboflavin"), and means for detecting and/or quantifying any current generated (FIG. 2 "electrode" & see **2.3 Electrochemical Measurements**, page 686 "Tacussel PRG-DEL potentiostat in conjunction with a Kipp and Zonen BD 91 XY/t recorder").

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 7, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over COSNIER et al. ("*An Original Electroenzymatic System: Flavin Reductase-Riboflavin for the Improvement of Dehydrogenase-Based Biosensors. Application to the Amperometric Detection of Lactate* " Electroanalysis Vol. 9 No. 9 (1997) pages 685-688) in view of WONG et al. (U.S. Patent 6,117,661).

a. With regards to claims 7, 9, and 10, independent claim 1 is clearly anticipated by COSNIER et al. under 35 U.S.C. 102(b) as discussed above. COSNIER et al. discloses a method for detecting the presence, absences, or concentration of NADH or NADPH in a sample comprising a reduction/oxidation sequence with a redox enzyme, reductase, and active redox agent. COSNIER et al. discloses a method wherein the reductase allows

transfer of electrons to/from the NADH or NADPH and the redox active agent (FIG. 2 "flavin reductase").

COSNIER et al. does not appear to explicitly disclose a method wherein the reductase, which allows two-electron transfer between the NADH/NADPH and the redox active agent, is specific to NADH and is a putidaredoxin reductase of the cytochrome $P450_{cam}$ enzyme system from pseudonomas putida.

However, WONG et al. discloses a composition to be a cytochrome $P450_{cam}$ from Pseudonomas putida (line 19-21, column 1). WONG et al. discloses the study of putidaredoxin reductase comprising the $P450_{cam}$ in an oxidation reaction with NADH as a co-factor (line 34-38, column 3). WONG et al. also discloses the reductase comprising the $P450_{cam}$ shows much higher turnover activities (line 43-45, column 3).

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the method, as disclosed by COSNIER et al., to include using putidaredoxin reductase comprising the $P450_{cam}$ which is specific to NADH, as disclosed by WONG et al., because WONG et al. suggest the application of the reductase in an oxidation reaction with NADH, because one with ordinary skill would have predicted success in the substitution of the putidaredoxin reductase comprising the $P450_{cam}$ in the method disclosed by COSNIER et al. based on the known properties shown by WONG et al. of the reductase in an oxidation reaction with NADH, and because the reductase, as disclosed by WONG et al., in combination with NADH yields higher turnover activities.

9. Claims 7, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over COSNIER et al. ("*An Original Electroenzymatic System: Flavin Reductase-Riboflavin for the Improvement of Dehydrogenase-Based Biosensors. Application to the Amperometric Detection of Lactate* " Electroanalysis Vol. 9 No. 9 (1997) pages 685-688) in view of FREDRICKS et al. ("*Stimulation of the Transhydrogenase Activity of Spinach Ferredoxin-Nicotinamide Adenine Dinucleotide Phosphate Reductase by Ferredoxin*" The Journal of Biological Chemistry Vol. 246 No. 5 (1971) pages 1201-1205).

a. With regards to claims 7, 11, and 12, independent claim 1 is clearly anticipated by COSNIER et al. under 35 U.S.C. 102(b) as discussed above. COSNIER et al. discloses a method for detecting the presence, absences, or concentration of NADH or NADPH in a sample comprising a reduction/oxidation sequence with a redox enzyme, reductase, and active redox agent. COSNIER et al. discloses a method wherein the reductase allows transfer of electrons to/from the NADH or NADPH and the redox active agent (FIG. 2 "flavin reductase").

COSNIER et al. does not appear to explicitly disclose a method wherein the reductase, which allows two-electron transfer between the NADH/NADPH and the redox active agent, is specific to NADPH and is spinach ferrodoxin reductase.

However, FREDRICKS et al. discloses a study of spinach ferrodoxin reductase with NADPH (1st paragraph, **SUMMARY**). As made evident by FREDRICKS et al., the application of spinach ferrodoxin reductase specified for NADPH is a conventional and known technique.

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the method, as disclosed by COSNIER et al., to include using spinach ferrodoxin reductase with NADPH as the reductase, as disclosed by FREDRICKS et al., because the application of spinach ferrodoxin is a conventional technique that one with ordinary skill would have predicted success in the substitution of the reductase disclosed by FREDRICKS et al. in the method disclosed by COSNIER et al. based on the known properties of spinach ferrodoxin reductase specified for NADPH.

9. Claims 8 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over COSNIER et al. ("*An Original Electroenzymatic System: Flavin Reductase-Riboflavin for the Improvement of Dehydrogenase-Based Biosensors. Application to the Amperometric Detection of Lactate* " Electroanalysis Vol. 9 No. 9 (1997) pages 685-688) in view of BU et al. ("*NAD(P)H Sensor Based on Enzyme Entrapment in Ferrocene-Containing Polycrylamide-Based Redox Gels*" Anal. Chem. Vol. 70 No. 20 (1998) pages 4320-4325).

a. With regards to claims 8 and 14, independent claim 1 is clearly anticipated by COSNIER et al. under 35 U.S.C. 102(b) as discussed above. COSNIER et al. discloses a method for detecting the presence, absences, or concentration of NADH or NADPH in a sample comprising a reduction/oxidation sequence with a redox enzyme, reductase, and active redox agent. COSNIER et al. discloses a method wherein the redox active agent accepts two-electrons from the reductase to transfer to the electrode (FIG. 2 "riboflavin").

COSNIER et al. does not appear to explicitly disclose a method wherein the redox active agent is ferricyanide ($Fe(CN)_6^{3-}$), which is not an organic dye.

However, BU et al. discloses a method for detecting NADH and NADPH and discloses a redox active agent for accepting two-electrons from a reductase to generate a current in an electrode (equation (1) & (2) of the 1st column, page 4321). BU et al. discloses known redox active agents can be ferricyanide (1st column, page 4321 after equations (1) & (2) "ferricyanide").

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the method, as disclosed by COSNIER et al., to include using ferricyanide as the redox active agent for accepting two-electrons from the reductase to transfer to the electrode, as disclosed by BU et al., because ferricyanide is a conventional redox active agent in an application to detect NADH and NADPH as made evident by BU et al. and because one with ordinary skill would have predicted success in the substitution of ferricyanide as the redox active agent in the method disclosed by COSNIER et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DUSTIN Q. DAM whose telephone number is (571)270-5120. The examiner can normally be reached on Monday through Thursday, 7:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on (571)272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

dd
April 16, 2008

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